#18



SEQUENCE LISTING

- <110> Sato, Taka-Aki Yanagisawa, Junn
- <120> COMPOUNDS THAT INHIBIT INTERACTION BETWEEN SIGNAL-TRANSDUCING PROTEINS AND THE GLGF (PDZ/DHR) DOMAIN AND USES THEREOF
- <130> 48962-A-PCT-US
- <140> 09/230,111
- <141> 1999-05-17
- <160> 33
- <170> PatentIn Ver. 2.1
- <210> 1
- <211> 4
- <212> PRT
- <213> Artificial Sequence
- <220>
- <223> Description of Artificial Sequence:source:synthesized
- <220>
- <221> SITE
- <222> (1)
- <223> Xaa=Gly, Ser, Ala or Glu
- <220>
- <221> SITE
- <222> (4)
- <223> Xaa=Phe, Ile or Leu
- <400> 1
- Xaa Leu Gly Xaa
 - 1
- <210> 2
- <211> 9
- <212> PRT
- <213> Artificial Sequence
- <220>

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<223> Description of Artificial
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<220>
<221> SITE
<222> (1)
<223> Xaa=Lys, Arg or Gln
<220>
<221> SITE
<222> (2)..(5)
<223> Xaa=any amino acid, up to 2 Xaa may be missing
<220>
<221> SITE
<222> (6)
<223> Xaa=Gly, Ser, Ala or Glu
<220>
<221> SITE
<222> (9)
<223> Xaa=Phe, Ile or Leu
<400> 2
Xaa Xaa Xaa Xaa Xaa Leu Gly Xaa
  1
<210> 3
<211> 4
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial
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<400> 3
Ser Leu Gly Ile
  1
<210> 4
<211> 3
<212> PRT
<213> Artificial Sequence
<220>
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<223> Description of Artificial
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<221> SITE
<222> (1)
<223> Xaa=Ser or Thr
<220>
<221> SITE
<222> (2)
<223> Xaa=any one amino acid
<220>
<221> SITE
<222> (3)
<223> Xaa=Val, Ile or Leu
<400> 4
Xaa Xaa Xaa
<210> 5
<211> 15
<212> PRT
<213> human
<400> 5
Asp Ser Glu Asn Ser Asn Phe Arg Asn Glu Ile Gln Ser Leu Val
                                                          15
                 5
                                     10
<210> 6
<211> 15
<212> PRT
<213> rat
<400> 6
Ser Ile Ser Asn Ser Arg Asn Glu Asn Glu Gly Gln Ser Leu Glu
                                     10
                 5
<210> 7
<211> 15
<212> PRT
<213> mouse
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<400> 7
  Ser Thr Pro Asp Thr Gly Asn Glu Asn Glu Gly Gln Cys Leu Glu
                                        10
<210> 8
  <211> 4
  <212> PRT
  <213> Artificial Sequence
  <220>
  <223> Description of Artificial
        Sequence:source:synthesized
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  Glu Ser Leu Val
    1
  <210> 9
  <211> 6
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  <223> Description of Artificial Sequence:
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  Thr Ile Gln Ser Val Ile
    1
                    5
  <210> 10
  <211> 8
  <212> PRT
  <213> Artificial Sequence
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  <223> Description of Artificial
        Sequence:source:synthesized
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  Arg Gly Phe Ile Ser Ser Leu Val
                    5
    1
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Δ

<210> 11

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<213> Artificial Sequence
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<223> Description of Artificial
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Arg Glu Thr Ile Glu Ser Thr Val
<210> 12
<211> 11
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<400> 12
Gln Asn Phe Arg Thr Tyr Ile Val Ser Phe Val
  1
                  5
<210> 13
<211> 13
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<400> 13
Ser Asp Ser Asn Met Asn Met Asn Glu Leu Ser Glu Val
  1
                  5
<210> 14
<211> 15
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial

Sequence:source:synthesized

| <400> | 14 | | | | | | | | |
|--------|-------------------------------|--------|-----|-------------|------|------|------|--|--|
| Pro P | ro Thr Cys Ser Gln Ala Asn Se | er Gly | Arg | Ile | Ser | Thr | Let | | |
| 1 | 5 | 10 | | | | | 15 | | |
| | | - | | | | | | | |
| | | | | | | | | | |
| <210> | 15 | | | | | | | | |
| <211> | 15 | | | | | | | | |
| <212> | PRT | | | | | | | | |
| <213> | Artificial Sequence | | | | | | | | |
| | | | | | | | | | |
| <220> | | | | | | | | | |
| <223> | Description of Artificial | | | | | | | | |
| | Sequence:source:synthesized | | | | | | | | |
| | | | | | | | | | |
| <400> | 15 | | | | | | | | |
| Ile A | sp Leu Ala Ser Glu Phe Leu Ph | ie Leu | Ser | Asn | Ser | Phe | Leu | | |
| 1 | 5 | 10 | | | | | 15 | | |
| | | | | | | | | | |
| | | | | | | | | | |
| <210> | 16 | | | | | | | | |
| <211> | 15 | | | | | | | | |
| <212> | PRT | | | | | | | | |
| <213> | Artificial Sequence | | | | | | | | |
| | | | | | | | | | |
| <220> | | | | | | | | | |
| <223> | Description of Artificial | | | | | | | | |
| | Sequence:source:synthesized | | | | | | | | |
| | | | | | | | | | |
| <400> | | | | | | | | | |
| Asp Se | er Glu Met Tyr Asn Phe Arg Se | | Leu | Ala | Ser | Val | | | |
| 1 | 5 | 10 | | | | | 15 | | |
| | | | | | | | | | |
| | | | | | | | | | |
| <210> | | | | | | | | | |
| <211> | | | | | | | | | |
| <212> | | | | | | | | | |
| <213> | Artificial Sequence | | | | | | | | |
| 200 | | | | | | | | | |
| <220> | | | | | | | | | |
| <223> | Description of Artificial | | | | | | | | |
| | Sequence:source:synthesized | | | | | | | | |
| 465 | | | | | | | | | |
| <400> | | - C3 | ~1 | c 1- | e | T.C. | 37~3 | | |
| Ile P | o Pro Asp Ser Glu Asp Gly As | n Giu | GIU | GIN | ser. | neu | 15 | | |
| | | 1.0 | | | | | | | |

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<210> 18
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial
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Gln Ser Leu Val
  1
<210> 19
<211> 5
<212> PRT
<213> Artificial Sequence
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<223> Description of Artificial Sequence:source
      synthesized
<400> 19
Ile Gln Ser Leu Val
 1
<210> 20
<211> 6
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial
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<400> 20
Glu Ile Gln Ser Leu Val
                  5
<210> 21
<211> 7
<212> PRT
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<213> Artificial Sequence

<220> <223> Description of Artificial Sequence:source:synthesized <400> 21 Asn Glu Ile Gln Ser Leu Val <210> 22 <211> 8 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence:source:synthesized <400> 22 Arg Asn Glu Ile Gln Ser Leu Val <210> 23 <211> 15 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence:source:synthesized <400> 23 Asp Ser Glu Asn Ser Asn Phe Arg Asn Glu Ile Gln Ser Leu Val 5 10 <210> 24 <211> 427 <212> PRT <213> human <400> 24

8

20

Met Gly Ala Gly Ala Thr Gly Arg Ala Met Asp Gly Pro Arg Leu Leu

Leu Leu Leu Leu Gly Val Ser Leu Gly Gly Ala Lys Glu Ala Cys

25

- Pro Thr Gly Leu Tyr Thr His Ser Gly Glu Cys Cys Lys Ala Cys Asn 35 40 45
- Leu Gly Glu Gly Val Ala Gln Pro Cys Gly Ala Asn Gln Thr Val Cys
 50 55 60
- Glu Pro Cys Leu Asp Ser Val Thr Phe Ser Asp Val Val Ser Ala Thr 65 70 75 80
- Glu Pro Cys Lys Pro Cys Thr Glu Cys Val Gly Leu Gln Ser Met Ser 85 90 95
- Ala Pro Cys Val Glu Ala Asp Asp Ala Val Cys Arg Cys Ala Tyr Gly
 100 105 110
- Tyr Tyr Gln Asp Glu Thr Thr Gly Arg Cys Glu Ala Cys Arg Val Cys 115 120 125
- Glu Ala Gly Ser Gly Leu Val Phe Ser Cys Gln Asp Lys Gln Asn Thr 130 135 140
- Val Cys Glu Glu Cys Pro Asp Gly Thr Tyr Ser Asp Glu Ala Asn His 145 150 155 160
- Val Asp Pro Cys Leu Pro Cys Thr Val Cys Glu Asp Thr Glu Arg Gln
 165 170 175
- Leu Arg Glu Cys Thr Arg Trp Ala Asp Ala Glu Cys Glu Glu Ile Pro 180 185 190
- Gly Arg Trp Ile Thr Arg Ser Thr Pro Pro Glu Gly Ser Asp Ser Thr 195 200 205
- Ala Pro Ser Thr Gln Glu Pro Glu Ala Pro Pro Glu Gln Asp Leu Ile 210 215 220
- Ala Ser Thr Val Ala Gly Val Val Thr Thr Val Met Gly Ser Ser Gln
 225 230 235 240
- Pro Val Val Thr Arg Gly Thr Thr Asp Asn Leu Ile Pro Val Tyr Cys 245 250 255
- Ser Ile Leu Ala Ala Val Val Gly Leu Val Ala Tyr Ile Ala Phe 260 265 270
- Lys Arg Trp Asn Ser Cys Lys Gln Asn Lys Gly Gly Ala Asn Ser Arg 275 280 285

Pro Val Asn Gln Thr Pro Pro Pro Glu Gly Glu Lys Ile His Ser Asp 290 295 300

Ser Gly Ile Ser Val Asp Ser Gln Ser Leu His Asp Gln Gln Pro His 305 310 315 320

Thr Gln Thr Ala Ser Gly Gln Ala Leu Lys Gly Asp Gly Gly Leu Tyr
325 330 335

Ser Ser Leu Pro Pro Ala Lys Arg Glu Glu Val Glu Lys Leu Leu Asn 340 345 350

Gly Ser Ala Gly Asp Thr Trp Arg His Leu Ala Gly Glu Leu Gly Tyr 355 360 365

Gln Pro Glu His Ile Asp Ser Phe Thr His Glu Ala Cys Pro Val Arg 370 375 380

Ala Leu Leu Ala Ser Trp Ala Thr Gln Asp Ser Ala Thr Leu Asp Ala 385 390 395 400

Leu Leu Ala Ala Leu Arg Arg Ile Gln Arg Ala Asp Leu Val Glu Ser 405 410 415

Leu Cys Ser Glu Ser Thr Ala Thr Ser Pro Val 420 425

<210> 25

<211> 458

<212> PRT

<213> human

<400> 25

Met Asn Arg Gly Val Pro Phe Arg His Leu Leu Leu Val Leu Gln Leu 1 5 10 15

Ala Leu Leu Pro Ala Ala Thr Gln Gly Lys Lys Val Val Leu Gly Lys
20 25 30

Lys Gly Asp Thr Val Glu Leu Thr Cys Thr Ala Ser Gln Lys Lys Ser 35 40 45

Ile Gln Phe His Trp Lys Asn Ser Asn Gln Ile Lys Ile Leu Gly Asn 50 55 60

Gln Gly Ser Phe Leu Thr Lys Gly Pro Ser Lys Leu Asn Asp Arg Ala

Asp Ser Arg Arg Ser Leu Trp Asp Gln Gly Asn Phe Pro Leu Ile Ile 85 90 95

Lys Asn Leu Lys Ile Glu Asp Ser Asp Thr Tyr Ile Cys Glu Val Glu 100 105 110

Asp Gln Lys Glu Glu Val Gln Leu Leu Val Phe Gly Leu Thr Ala Asn 115 120 125

Ser Asp Thr His Leu Leu Gln Gly Gln Ser Leu Thr Ile Thr Leu Glu 130 135 140

Ser Pro Pro Gly Ser Ser Pro Ser Val Gln Cys Arg Ser Pro Arg Gly
145 150 155 160

Lys Asn Ile Gln Gly Gly Lys Thr Leu Ser Val Ser Gln Leu Glu Leu 165 170 175

Gln Asp Ser Gly Thr Trp Thr Cys Thr Val Leu Gln Asn Gln Lys Lys 180 185 190

Val Glu Phe Lys Ile Asp Ile Val Val Leu Ala Phe Gln Lys Ala Ser 195 200 205

Ser Ile Val Tyr Lys Lys Glu Gly Glu Gln Val Glu Phe Ser Phe Pro 210 215 220

Leu Ala Phe Thr Val Glu Lys Leu Thr Gly Ser Gly Glu Leu Trp Trp 225 230 235 240

Gln Ala Glu Arg Ala Ser Ser Ser Lys Ser Trp Ile Thr Phe Asp Leu 245 250 255

Lys Asn Lys Glu Val Ser Val Lys Arg Val Thr Gln Asp Pro Lys Leu 260 265 270

Gln Met Gly Lys Lys Leu Pro Leu His Leu Thr Leu Pro Gln Ala Leu 275 280 285

Pro Gln Tyr Ala Gly Ser Gly Asn Leu Thr Leu Ala Leu Glu Ala Lys 290 295 300

Thr Gly Lys Leu His Gln Glu Asn Val Leu Val Val Met Arg Ala Thr 305 310 315 320

Gln Leu Gln Lys Asn Leu Thr Cys Glu Val Trp Gly Pro Thr Ser Pro

325 330 335

Lys Leu Met Leu Ser Leu Lys Leu Glu Asn Lys Glu Ala Lys Val Ser 340 345 350

Lys Arg Glu Lys Ala Val Trp Val Leu Asn Pro Glu Ala Gly Met Trp 355 360 365

Gln Cys Leu Leu Ser Asp Ser Gly Gln Val Leu Leu Glu Ser Asn Ile 370 375 380

Lys Val Leu Pro Thr Trp Ser Thr Pro Val Gln Pro Met Ala Leu Ile 385 390 395 400

Val Leu Gly Gly Val Ala Gly Leu Leu Leu Phe Ile Gly Leu Gly Ile 405 410 415

Phe Phe Cys Val Arg Cys Arg His Arg Arg Arg Gln Ala Glu Arg Met 420 425 430

Ser Gln Ile Lys Arg Leu Leu Ser Glu Lys Lys Glu Cys Gln Cys Pro 435 440 445

His Arg Phe Gln Lys Thr Cys Ser Pro Ile 450 455

<210> 26

<211> 828

<212> PRT

<213> human

<400> 26

Met Asn Ser Gly Val Ala Met Lys Tyr Gly Asn Asp Ser Ser Ala Glu
1 5 10 15

Leu Ser Glu Leu His Ser Ala Ala Leu Ala Ser Leu Lys Gly Asp Ile 20 25 30

Val Glu Leu Asn Lys Arg Leu Gln Gln Thr Glu Arg Glu Asp Leu Leu 35 40 45

Glu Lys Lys Leu Ala Lys Ala Gln Cys Glu Gln Ser His Leu Met Arg
50 55 60

Glu His Glu Asp Val Gln Glu Arg Thr Thr Leu Arg Tyr Glu Glu Arg
65 70 75 80

- Ile Thr Glu Leu His Ser Val Ile Ala Glu Leu Asn Lys Lys Ile Asp
 85 90 95
- Arg Leu Gln Gly Thr Thr Ile Arg Glu Glu Asp Glu Tyr Ser Glu Leu 100 105 110
- Arg Ser Glu Leu Ser Gln Ser Gln His Glu Val Asn Glu Asp Ser Arg 115 120 125
- Ser Met Asp Gln Asp Gln Thr Ser Val Ser Ile Pro Glu Asn Gln Ser 130 135 140
- Thr Met Val Thr Ala Asp Met Asp Asn Cys Ser Asp Ile Asn Ser Glu 145 150 155 160
- Leu Gln Arg Val Leu Thr Gly Leu Glu Asn Val Val Cys Gly Arg Lys
 165 170 175
- Lys Ser Ser Cys Ser Leu Ser Val Ala Glu Val Asp Arg His Ile Glu 180 185 190
- Gln Leu Thr Thr Ala Ser Glu His Cys Asp Leu Ala Ile Lys Thr Val

 195 200 205
- Glu Glu Ile Glu Gly Val Leu Gly Arg Asp Leu Tyr Pro Asn Leu Ala 210 215 220
- Glu Glu Arg Ser Arg Trp Glu Lys Glu Leu Ala Gly Leu Arg Glu Glu 225 230 235 240
- Asn Glu Ser Leu Thr Ala Met Leu Cys Ser Lys Glu Glu Glu Leu Asn 245 250 255
- Arg Thr Lys Ala Thr Met Asn Ala Ile Arg Glu Glu Arg Asp Arg Leu 260 265 270
- Arg Arg Val Arg Glu Leu Gln Thr Arg Leu Gln Ser Val Gln Ala 275 280 285
- Thr Gly Pro Ser Ser Pro Gly Arg Leu Thr Ser Thr Asn Arg Pro Ile 290 295 300
- Asn Pro Ser Thr Gly Glu Leu Ser Thr Ser Ser Ser Asn Asp Ile 305 310 315 320
- Pro Ile Ala Lys Ile Ala Glu Arg Val Lys Leu Ser Lys Thr Arg Ser 325 330 335

- Glu Ser Ser Ser Asp Arg Pro Val Leu Gly Ser Glu Ile Ser Ser 340 345 350
- Ile Gly Val Ser Ser Ser Val Ala Glu His Leu Ala His Ser Leu Gln 355 360 365
- Asp Cys Ser Asn Ile Gln Glu Ile Phe Gln Thr Leu Tyr Ser His Gly 370 375 380
- Ser Ala Ile Ser Glu Ser Lys Ile Arg Glu Phe Glu Val Glu Thr Glu 385 390 395 400
- Arg Leu Asn Ser Arg Ile Glu His Leu Lys Ser Gln Asn Asp Leu Leu 405 410 415
- Thr Ile Thr Leu Glu Glu Cys Lys Ser Asn Ala Glu Arg Met Ser Met 420 425 430
- Leu Val Gly Lys Tyr Glu Ser Asn Ala Thr Ala Leu Arg Leu Ala Leu 435 440 445
- Gln Tyr Ser Glu Gln Cys Ile Glu Ala Tyr Glu Leu Leu Leu Ala Leu 450 455 460
- Ala Glu Ser Glu Gln Ser Leu Ile Leu Gly Gln Phe Arg Ala Ala Gly 465 470 475 480
- Val Gly Ser Ser Pro Gly Asp Gln Ser Gly Asp Glu Asn Ile Thr Gln 485 490 495
- Met Leu Lys Arg Ala His Asp Cys Arg Lys Thr Ala Glu Asn Ala Ala 500 505 510
- Lys Ala Leu Leu Met Lys Leu Asp Gly Ser Cys Gly Gly Ala Phe Ala 515 520 525
- Val Ala Gly Cys Ser Val Gln Pro Trp Glu Ser Leu Ser Ser Asn Ser 530 535 540
- His Thr Ser Thr Thr Ser Ser Thr Ala Ser Ser Cys Asp Thr Glu Phe 545 550 555 560
- Thr Lys Glu Asp Glu Gln Arg Leu Lys Asp Tyr Ile Gln Gln Leu Lys 565 570 575
- Asn Asp Arg Ala Ala Val Lys Leu Thr Met Leu Glu Leu Glu Ser Ile 580 585 590

His Ile Asp Pro Leu Ser Tyr Asp Val Lys Pro Arg Gly Asp Ser Gln 595 600 605

Arg Leu Asp Leu Glu Asn Ala Val Leu Met Gln Glu Leu Met Ala Met 610 620

Lys Glu Glu Met Ala Glu Leu Lys Ala Gln Leu Tyr Leu Leu Glu Lys 625 630 635 640

Glu Lys Lys Ala Leu Glu Leu Lys Leu Ser Thr Arg Glu Ala Gln Glu 645 650 655

Gln Ala Tyr Leu Val His Ile Glu His Leu Lys Ser Glu Val Glu Glu 660 665 670

Gln Lys Glu Gln Arg Met Arg Ser Leu Ser Ser Thr Ser Ser Gly Ser 675 680 685

Lys Asp Lys Pro Gly Lys Glu Cys Ala Asp Ala Ala Ser Pro Ala Leu 690 695 700

Ser Leu Ala Glu Leu Arg Thr Thr Cys Ser Glu Asn Glu Leu Ala Ala 705 710 715 720

Glu Phe Thr Asn Ala Ile Arg Arg Glu Lys Lys Leu Lys Ala Arg Val 725 730 735

Gln Glu Leu Val Ser Ala Leu Glu Arg Leu Thr Lys Ser Ser Glu Ile 740 745 750

Arg His Gln Gln Ser Ala Glu Phe Val Asn Asp Leu Lys Arg Ala Asn 755 760 765

Ser Asn Leu Val Ala Ala Tyr Glu Lys Ala Lys Lys Lys His Gln Asn 770 775 780

Lys Leu Lys Lys Leu Glu Ser Gln Met Met Ala Met Val Glu Arg His 785 790 795 800

Glu Thr Gln Val Arg Met Leu Lys Gln Arg Ile Ala Leu Leu Glu Glu 805 810 815

Glu Asn Ser Arg Pro His Thr Asn Glu Thr Ser Leu 820 825

<210> 27 <211> 672

<212> PRT <213> human

<400> 27

- Met Ala Asp Val Phe Pro Gly Asn Asp Ser Thr Ala Ser Gln Asp Val 1 5 10 15
- Ala Asn Arg Phe Ala Arg Lys Gly Ala Leu Arg Gln Lys Asn Val His
 20 25 30
- Glu Val Lys Asp His Lys Phe Ile Ala Arg Phe Phe Lys Gln Pro Thr 35 40 45
- Phe Cys Ser His Cys Thr Asp Phe Ile Trp Gly Phe Gly Lys Gly Gly 50 55 60
- Phe Gln Cys Gln Val Cys Cys Phe Val Val His Lys Arg Cys His Glu 65 70 75 80
- Phe Val Thr Phe Ser Cys Pro Gly Ala Asp Lys Gly Pro Asp Thr Asp 85 90 95
- Asp Pro Arg Ser Lys His Lys Phe Lys Ile His Thr Tyr Gly Ser Pro 100 105 110
- Thr Phe Cys Asp His Cys Gly Ser Leu Leu Tyr Gly Leu Ile His Gln
 115 120 125
- Gly Met Lys Cys Asp Thr Cys Asp Met Asn Val His Lys Gln Cys Val 130 135 140
- Ile Asn Val Pro Ser Leu Cys Gly Met Asp His Thr Glu Lys Arg Gly
 145 150 155 160
- Arg Ile Tyr Leu Lys Ala Glu Val Ala Asp Glu Lys Leu His Val Thr 165 170 175
- Val Arg Asp Ala Lys Asn Leu Ile Pro Met Asp Pro Asn Gly Leu Ser 180 185 190
- Asp Pro Tyr Val Lys Leu Lys Leu Ile Pro Asp Pro Lys Asn Glu Ser 195 200 205
- Lys Gln Lys Thr Lys Thr Ile Arg Ser Thr Leu Asn Pro Gln Trp Asn 210 215 220
- Glu Ser Phe Thr Phe Lys Leu Lys Pro Ser Asp Lys Asp Arg Arg Leu 225 230 235 240

- Ser Val Glu Ile Trp Asp Trp Asp Arg Thr Thr Arg Asn Asp Phe Met 245 250 255
- Gly Ser Leu Ser Phe Gly Val Ser Glu Leu Met Lys Met Pro Ala Ser 260 265 270
- Gly Trp Tyr Lys Leu Leu Asn Gln Glu Glu Glu Glu Tyr Tyr Asn Val 275 280 285
- Pro Ile Pro Glu Gly Asp Glu Glu Gly Asn Met Glu Leu Arg Gln Lys 290 295 300
- Phe Glu Lys Ala Lys Leu Gly Pro Ala Gly Asn Lys Val Ile Ser Pro 305 310 315 320
- Ser Glu Asp Arg Lys Gln Pro Ser Asn Asn Leu Asp Arg Val Lys Leu 325 330 335
- Thr Asp Phe Asn Phe Leu Met Val Leu Gly Lys Gly Ser Phe Gly Lys 340 345 350
- Val Met Leu Ala Asp Arg Lys Gly Thr Glu Glu Leu Tyr Ala Ile Lys 355 360 365
- Ile Leu Lys Lys Asp Val Val Ile Gln Asp Asp Val Glu Cys Thr 370 375 380
- Met Val Glu Lys Arg Val Leu Ala Leu Leu Asp Lys Pro Pro Phe Leu 385 390 395 400
- Thr Gln Leu His Ser Cys Phe Gln Thr Val Asp Arg Leu Tyr Phe Val
 405 410 415
- Met Glu Tyr Val Asn Gly Gly Asp Leu Met Tyr His Ile Gln Gln Val 420 425 430
- Gly Lys Phe Lys Glu Pro Gln Ala Val Phe Tyr Ala Ala Glu Ile Ser 435 440 445
- Ile Gly Leu Phe Phe Leu His Lys Arg Gly Ile Ile Tyr Arg Asp Leu 450 455 460
- Lys Leu Asp Asn Val Met Leu Asp Ser Glu Gly His Ile Lys Ile Ala 465 470 475 480
- Asp Phe Gly Met Cys Lys Glu His Met Met Asp Gly Val Thr Thr Arg
 485 490 495

Thr Phe Cys Gly Thr Pro Asp Tyr Ile Ala Pro Glu Ile Ile Ala Tyr
500 505 510

Gln Pro Tyr Gly Lys Ser Val Asp Trp Trp Ala Tyr Gly Val Leu Leu 515 520 525

Tyr Glu Met Leu Ala Gly Gln Pro Pro Phe Asp Gly Glu Asp Glu Asp 530 535 540

Glu Leu Phe Gln Ser Ile Met Glu His Asn Val Ser Tyr Pro Lys Ser 545 550 555 560

Leu Ser Lys Glu Ala Val Ser Ile Cys Lys Gly Leu Met Thr Lys His 565 570 575

Pro Ala Lys Arg Leu Gly Cys Gly Pro Glu Gly Glu Arg Asp Val Arg 580 585 590

Glu His Ala Phe Phe Arg Arg Ile Asp Trp Glu Lys Leu Glu Asn Arg 595 600 605

Glu Ile Gln Pro Pro Phe Lys Pro Lys Val Cys Gly Lys Gly Ala Glu 610 620

Asn Phe Asp Lys Phe Phe Thr Arg Gly Gln Pro Val Leu Thr Pro Pro 625 630 635 640

Asp Gln Leu Val Ile Ala Asn Ile Asp Gln Ser Asp Phe Glu Gly Phe 645 650 655

Ser Tyr Val Asn Pro Gln Phe Val His Pro Ile Leu Gln Ser Ala Val 660 665 670

<210> 28

<211> 471

<212> PRT

<213> human

<400> 28

Met Asp Ile Leu Cys Glu Glu Asn Thr Ser Leu Ser Ser Thr Thr Asn 1 5 10 15

Ser Leu Met Gln Leu Asn Asp Asp Thr Arg Leu Tyr Ser Asn Asp Phe

| As | n Ser | Gly 35 | | Ala | . Asn | Thr | Ser 40 | | Ala | Phe | Asn | Trp 45 | | Val | Asp |
|------------------------|--------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Se | r Glu 50 | | Arg | Thr | Asn | Leu 55 | Ser | Сув | Glu | Gly | Сув 60 | Leu | Ser | Pro | Ser |
| Су 6 | s Leu 5 | Ser | Leu | Leu | His 70 | Leu | Gln | Glu | Lys | Asn 75 | Trp | Ser | Ala | Leu | Leu 80 |
| Th | r Ala | Val | Val | Ile 85 | Ile | Leu | Thr | Ile | Ala 90 | Gly | Asn | Ile | Leu | Val 95 | Ile |
| Me | t Ala | Val | Ser 100 | Leu | Glu | Lys | Lys | Leu 105 | Gln | Asn | Ala | Thr | Asn 110 | Tyr | Phe |
| Le | u Met | Ser 115 | Leu | Ala | Ile | Ala | Asp 120 | Met | Leu | Leu | Gly | Phe 125 | Leu | Val | Met |
| Pro | 0 Val 130 | Ser | Met | Leu | Thr | Ile 135 | Leu | Tyr | Gly | Tyr | Arg 140 | Trp | Pro | Leu | Pro |
| Se: | r Lys 5 | Leu | Сув | Ala | Val 150 | Trp | Ile | Tyr | Leu | Asp 155 | Val | Leu | Phe | Ser | Thr 160 |
| Ala | a Ser | Ile | Met | His 165 | Leu | Сув | Ala | Ile | Ser 170 | Leu | Asp | Arg | Туг | Val 175 | Ala |
| Ile | e Gln | Asn | Pro 180 | Ile | His | His | Ser | Arg 185 | Phe | Asn | Ser | Arg | Thr 190 | Lys | Ala |
| Phe | e Leu | Lys 195 | Ile | Ile | Ala | Val | Trp 200 | Thr | Ile | Ser | Val | Gly 205 | Ile | Ser | Met |
| Pro | 210 | Pro | Val | Phe | Gly | Leu 215 | Gln | Asp | Asp | Ser | Lys 220 | Val | Phe | Lys | Glu |
| Gl ₃ 229 | y Ser | Сув | Leu | Leu | Ala 230 | Asp | Asp | Asn | Phe | Val 235 | Leu | Ile | Gly | Ser | Phe 240 |
| Va] | l Ser | Phe | Phe | Ile 245 | Pro | Leu | Thr | Ile | Met 250 | Val | Ile | Thr | Tyr | Phe 255 | Leu |
| Thi | r Ile | Lys | Ser | Leu | Gln | Lys | Glu | Ala | Thr | Leu | Сув | Val | Ser | Asp | Leu |

Gly Thr Arg Ala Lys Leu Ala Ser Phe Ser Phe Leu Pro Gln Ser Ser

275 280 285

Leu Ser Ser Glu Lys Leu Phe Gln Arg Ser Ile His Arg Glu Pro Gly 290 295 300

Ser Tyr Thr Gly Arg Arg Thr Met Gln Ser Ile Ser Asn Glu Gln Lys 305 310 315 320

Ala Cys Lys Val Leu Gly Ile Val Phe Phe Leu Phe Val Val Met Trp
325 330 335

Cys Pro Phe Phe Ile Thr Asn Ile Met Ala Val Ile Cys Lys Glu Ser 340 345 350

Cys Asn Glu Asp Val Ile Gly Ala Leu Leu Asn Val Phe Val Trp Ile 355 360 365

Gly Tyr Leu Ser Ser Ala Val Asn Pro Leu Val Tyr Thr Leu Phe Asn 370 375 380

Lys Thr Tyr Arg Ser Ala Phe Ser Arg Tyr Ile Gln Cys Gln Tyr Lys 385 390 395 400

Glu Asn Lys Lys Pro Leu Gln Leu Ile Leu Val Asn Thr Ile Pro Ala 405 410 415

Leu Ala Tyr Lys Ser Ser Gln Leu Gln Met Gly Gln Lys Lys Asn Ser 420 425 430

Lys Gln Asp Ala Lys Thr Thr Asp Asn Asp Cys Ser Met Val Ala Leu 435 440 445

Gly Lys Gln His Ser Glu Glu Ala Ser Lys Asp Asn Ser Asp Gly Val 450 455 460

Asn Glu Lys Val Ser Cys Val 465 470

<210> 29

<211> 481

<212> PRT

<213> human

<400> 29

Met Ala Leu Ser Tyr Arg Val Ser Glu Leu Gln Ser Thr Ile Pro Glu
1 5 10 15

- His Ile Leu Gln Ser Thr Phe Val His Val Ile Ser Ser Asn Trp Ser 20 25 30
- Gly Leu Gln Thr Glu Ser Ile Pro Glu Glu Met Lys Gln Ile Val Glu 35 40 45
- Glu Gln Gly Asn Lys Leu His Trp Ala Ala Leu Leu Ile Leu Met Val 50 55 60
- Ile Ile Pro Thr Ile Gly Gly Asn Thr Leu Val Ile Leu Ala Val Ser 65 70 75 80
- Leu Glu Lys Lys Leu Gln Tyr Ala Thr Asn Tyr Phe Leu Met Ser Leu 85 90 95
- Ala Val Ala Asp Leu Leu Val Gly Leu Phe Val Met Pro Ile Ala Leu 100 105 110
- Leu Thr Ile Met Phe Glu Ala Met Trp Pro Leu Pro Leu Val Leu Cys
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Cys Asn Gln Thr Thr Leu Gln Met Leu Glu Ile Phe Val Trp Ile 355 360 365

Gly Tyr Val Ser Ser Gly Val Asn Pro Leu Val Tyr Thr Leu Phe Asn 370 375 380

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- Glu Ala Glu Arg Ser Ser Gln Asn Lys His Glu Thr Gly Ser His Asp 245 250 255

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- Leu Leu Gly Asn Ser Arg Gly Ser Lys Glu Ala Arg Ala Arg Ala Ser 370 375 380
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 - Leu Arg Arg Tyr Ala Gly Met Ala Leu Thr Asn Leu Thr Phe Gly Asp 500 505 510

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- Asp Lys Leu Pro Asn Asn Glu Asp Arg Val Arg Gly Ser Phe Ala Phe 1825 1830 1835 1840
- Asp Ser Pro His His Tyr Thr Pro Ile Glu Gly Thr Pro Tyr Cys Phe 1845 1850 1855
- Ser Arg Asn Asp Ser Leu Ser Ser Leu Asp Phe Asp Asp Asp Asp Val 1860 1865 1870
- Asp Leu Ser Arg Glu Lys Ala Glu Leu Arg Lys Ala Lys Glu Asn Lys 1875 1880 1885
- Glu Ser Glu Ala Lys Val Thr Ser His Thr Glu Leu Thr Ser Asn Gln 1890 1895 1900
- Gln Ser Ala Asn Lys Thr Gln Ala Ile Ala Lys Gln Pro Ile Asn Arg 1905 1910 1915 1920
- Gly Gln Pro Lys Pro Ile Leu Gln Lys Gln Ser Thr Phe Pro Gln Ser 1925 1930 1935
- Ser Lys Asp Ile Pro Asp Arg Gly Ala Ala Thr Asp Glu Lys Leu Gln 1940 1945 1950
- Asn Phe Ala Ile Glu Asn Thr Pro Val Cys Phe Ser His Asn Ser Ser 1955 1960 1965
- Leu Ser Ser Leu Ser Asp Ile Asp Gln Glu Asn Asn Asn Lys Glu Asn 1970 1975 1980
- Glu Pro Ile Lys Glu Thr Glu Pro Pro Asp Ser Gln Gly Glu Pro Ser 1985 1990 1995 2000
- Lys Pro Gln Ala Ser Gly Tyr Ala Pro Lys Ser Phe His Val Glu Asp 2005 2010 2015
- Thr Pro Val Cys Phe Ser Arg Asn Ser Ser Leu Ser Ser Leu Ser Ile 2020 2025 2030
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